

Remarks

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks. Claims 15-40 are withdrawn. Claims 6-8, 12, 41-63, 65, and 66 are canceled. Claims 1-5, 9-11, 13-40, 64, 67 and 68 remain pending. Claims 1, 64, and 68 are independent.

Cited Art

The Action cites Kahn et al., "Laser Scanning Confocal Microscopy and Factor Analysis of Biomedical Image Sequences to Detect and Characterise HPV DNA sequences by FISH in HeLa Cells, Cytometry 28:269-279, 1997 ("Kahn").

Claims Rejections 35 USC § 112

Claims 1-5, 9-11, 13, 14, 64, and 67 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinction claim the subject matter which applicant regards as the invention.

Claims 1 and 64 are rejected as having insufficient basis for "the confocal microscope." Because "a confocal microscope" appears in line 3 of the claims, there is sufficient antecedent basis. Accordingly, the rejection can be withdrawn. Claims 2-5, 9-11, 13, 14, and 67 were included in the rejection because they depend from claim 1.

Applicants acknowledge the rejection of claim 5 and have amended so that it now depends from claim 4. So, the rejection can now be withdrawn.

Claims Rejections 35 USC § 102

Claims 1-5, 9-11, 13, 14, 64, 67, and 68 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kahn. Applicants respectfully disagree. For clarification of claim 1, Applicants have added the following language:

wherein the automatically-counted test signals from the test probe comprise at least two distinguished spatially overlapping nucleic acid probe signals in the biological specimen.

The language finds support, for example, at FIGS. 9B and 9C, which are described in the application at page 22, lines 17 et seq. and page 29, lines 29 et seq. The amendment does not

necessarily narrow the claim, but clarifies that at least two of the counted signals are spatially overlapping. Applicants believe the claim clearly distinguishes over Kahn.

Kahn's description of iterative algorithms does not anticipate automatically counting a number of test signals or automatically counting a number of reference signals as recited by claim 1. The Action reads claim 1's "test" and "reference" signals on Kahn's description of hybridization signals specific to the spectrum of Fast Red (FR) and cell nuclei counterstained with thiazole orange (TO). However, even if the logic of the Action is followed, Kahn still fails to describe the recited counting step. The Action relies on Kahn's description iterative algorithms in the last paragraph of page 277 as anticipating the claimed arrangement (emphasis added):

The second step, called oblique analysis, aims to estimate factors representing the fundamental curves. After the orthogonal analysis, each curve is a linear combination of the two or three first singular vectors; but these vectors have no physical meanings. Due to orthogonal conditions, they have both positive and negative values and cannot be considered as extinction velocities, spectral curves, or depth emission profiles. *Iterative algorithms have been proposed to find an appropriate solution, i.e., factors with physical meanings and positive weights of the curves on these factors (7, 1).* The initial solution is directly determined from the set of experimental curves. Therefore, factors are estimated from the experimental data, as well as globally, and do not depend on spatial locations.

Although Kahn does describe that iterative algorithms have been proposed to find factors with physical meanings, it requires impermissible hindsight to conclude that "factors with physical meanings" discloses counting signals as recited. Kahn's description could mean any number of arrangements other than counting, so counting is not inherent in Kahn.

Further, even if Kahn could somehow be read as disclosing counting, Kahn still fails to anticipate "determining a ratio of automatically-counted test signals from the test probe to the automatically-counted reference signals from the reference probe" as recited by claim 1. The Action describes that Kahn determines a ratio of TO and FR intensities. However, Applicants can find no such description in Kahn. Kahn does mention intensities in a number places. For example, at paragraph 6 of page 277, Kahn describes:

Pixels of the images are combined into small squared clusters (8 x 8 pixels). Fluorescent image intensity curves are computed for each cluster and define the columns of an $N \times P$ rectangular matrix, denoted X , where N is the total number of images in the sequence, and P , the total number of clusters.

Thus, Kahn does describe computing image intensity curves, but it does not describe computing a ratio for the curves. Further, even if Kahn did have such a description, it would not necessarily anticipate "determining a ratio of the automatically-counted test signals" because a ratio of intensities would not anticipate a ratio for counted signals.

Claim 1's language concerning "distinguishing spatially overlapping nucleic acid probe signals" cannot be read out of the claim. Applicants point out that the claim explicitly recites, "distinguishing spatially overlapping nucleic acid probe signals." In paragraph 2 of page 279, Kahn discloses:

Further work needs to be undertaken to quantify these hybridization spots. Additional studies will be conducted (1) to combine sequences of images into 4D sequences by spectral selection at emission or by constant scanning time, and by altering the (z) position; and (2) to process these 4D sequences through FAMIS to distinguish targets by their spectrum or extinction velocity on optimized planes of observation.

So, even if Kahn could be read as teaching counting, Kahn makes no mention of distinguishing overlapping signals as recited. Kahn did not aim to distinguish spatially overlapping signals, so it can provide no guidance to a solution such as that found by the inventors.

In fact, Kahn's description of factors that "do not depend on spatial locations" teaches away from the recited "distinguishing spatially overlapping nucleic acid probe signals" recited by claim 1. In the abstract and in the last paragraph of page 273, Kahn does describe, "Factor images correspond to spatial distributions of the different factors." However, Kahn would lead one of ordinary skill to a solution that does not involve distinguishing spatially overlapping nucleic acid probe signals because it describes a solution with factors that "do not depend on spatial locations" at the top of page 278.

Claims 64 and 68 have similar language and are therefore also allowable at this time along with claim 1 and its dependent claims, 2-5, 9-11, 13-40, and 67.

Remaining Claims

Without belaboring the language of the dependent claims, Applicants point out that they each recite novel and non-obvious combinations not taught by Kahn.

Request for Interview

If any issues remain, the Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicants submit the foregoing formal Amendment so that the Examiner may fully evaluate Applicants' position, thereby enabling the interview to be more focused.

This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by a written request.

Conclusion


The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

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